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EXAMINER	
WOLLENBERGER, LOUIS V	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	10/826,130	KAYKAS ET AL.	
	Examiner	Art Unit	
	Louis V. Wollenberger	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *17-32 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/23/04, 11/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1–16 and 33 in the reply filed on July 15, 2005, is acknowledged. Applicants traverse the Restriction Requirement with respect to claim Groups I, II, and III on the grounds that it does not impose an undue burden on the Examiner to search and examine Claim Groups I, II, and III together. Groups II and III are related to Group I as process and product.

The reasons for distinctness among the three groups have previously been set forth in the restriction requirement mailed on June 28, 2005. As for applicants' contention that no search burden exists, attention is drawn to page 5 of the restriction requirement, which states that a burden exists because the searches required are divergent and not coextensive.

In the instant case, prior art searches of an expression vector (Group I) are not coextensive with prior art searches of a method for inhibiting gene expression (Group II) or with a method of determining the effect of an siRNA on a biological process (Group III) or to methods for identifying an siRNA that affects a biological process. Although a search of the vector of Group I may locate some literature relevant to the claimed methods, it may not necessarily retrieve all literature relevant to the method claims.

An adequate search of each of these inventions would require different key word searches of each structural and functional limitation in the vector and of each distinctive step of the methods using divergent patent and non-patent literature databases. The different searches would

then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious burden on the Office in terms of both search and examination.

As such, it would be burdensome to perform examination of inventions I, II, and III together. The restriction requirement is still deemed proper and is therefore made FINAL.

Status of the application

Claims 1–34 are pending. Claims 17–32 and 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 15, 2005.

Specification

The attempt to incorporate subject matter into this application by reference to a company catalog is ineffective because the catalog incorporated is unavailable or and not readily obtained. On page 11 of the instant application, applicants incorporate by reference the 2002-03 New England Biolabs Catalog & Technical Reference. As the 2002-03 catalog is unavailable to the examiner, and applicants have not provided the catalog, the examiner is unable to rely on this information for purposes of examination of the instant application.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (line 3, page 23 of the instant application). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claims

The examiner notes that Claim 3 of the instant application is unclear. Claim 3 recites the vector or Claim 2 "further comprising" a recognition site for a restriction enzyme, wherein the cleavage site for the enzyme is located outside the recognition site for the enzyme. These recitations are confusing in light of the earlier recitations in Claim 2, which recites the vector or Claim 1 "further comprising" a cleavage site for a restriction enzyme [...]. Because Claim 3 depends from Claim 2, it is unclear as to which cleavage sites and restriction enzymes applicants are referring to in Claim 3. Moreover, if the vector of claim 2 comprises a cleavage site for an enzyme, the vector inherently comprises a recognition site for that enzyme. Why then would it "further comprise" a recognition site, as recited in Claim 3? Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 6–16 are rejected under 35 U.S.C. 102(b) as being anticipated by Lois-Caballe et al (US 2003/0068821).

Claim 1 is drawn to an expression vector comprising first and second RNA polymerase III promoters operably associated with first and second RNA polymerase III termination signals, wherein the first and second RNA polymerase III promoters are oriented to promote bidirectional transcription of an insert disposed between the first and the second RNA polymerase III termination signals. Dependent Claim 6 recites the vector of Claim1 further comprising an insert disposed between the first and second RNA polymerase III termination signals. Dependent Claims 7 and 8 limit the size of the insert to between 19 and 29 nucleotides or between 19 and 23 nucleotides. Dependent Claim 9 recites the vector of Claim 1 further comprising a selectable marker operable in a eukaryotic cell. Dependent Claim 10 recites the vector of Claim 1 further comprising an origin of replication. Dependent Claims 11, 12 and 13 require that the vector of Claim 1 is either a plasmid vector, a viral vector or a linear vector.

Claim 14, an independent claim, recites a "plurality" of expression vectors, each comprising first and second RNA polymerase III promoters operably associated with first and second RNA polymerase III termination signals, and an insert disposed between the termination signals, wherein the first and second RNA polymerase III promoters are oriented to promote bidirectional transcription of the insert. Claims 15 and 16 limit claim 14 by stating that the insert is between 19 and 29 nucleotides (Claim 15) or between 19 and 23 nucleotides (Claim 16).

For purposes of examination, the phrase "a plurality of expression vectors," as used in Claim 14, is interpreted to mean more than one expression vector. The phrase "a plurality" does not require that the vectors be structurally distinct. Thus, Claims 6 and 14 are drawn to structurally identical vectors. Moreover, a recombinant DNA procedure used to construct a vector according to Claim 6, using conventional techniques of DNA synthesis, ligation, and

transformation would necessarily result in the production of multiple copies of the vector—i.e., a plurality of vectors—as recited in Claim 14.

The recitation "a selectable marker operable in a eukaryotic cell" in Claim 9 is interpreted in light of applicants' specification (page 11, lines 10–20), which states that:

> Vectors according to the invention may include various selection markers and/or reporter genes. These may be used for selection in the bacterial system the plasmids are grown in, but also for selection of transfected cells. Examples of reporter genes which may be employed to identify transfected cell lines include alkaline phosphatase (AP), beta galactosidase (LacZ), beta glucoronidase (GUS), chloramphenicol acetyltransferase (CAT), green fluorescent protein (GFP), horseradish peroxidase IHRPI, and luciferase (Luc). Exemplary antibiotic selectable markers include those that confer resistance to ampicillin, bleomycin, chlormmphenicol, gentomycin, hygromycin, kanamycin, lincomycin, methotrexate, phosphinothricin, puromycin, zeocin, and tetracyclin. The vectors of the invention may also include hybrid selection marker/reporter genes, such as a zeocin/GFP hybrid gene.

Regarding claims 1, 6–8, and 11–13 of the instant application, Lois-Caballe et al. teach a retroviral expression vector construct (specifically a lentiviral expression vector) comprising a first RNA pol III promoter operably linked to a first RNA coding region (the insert), and a second RNA pol III promoter operably linked to the same first RNA coding region in the opposite direction, such that expression of the RNA coding region from the first RNA pol III promoter results in a synthesis of a first RNA molecule as the sense strand and expression of the RNA coding region from the second RNA pol III promoter results in synthesis of a second RNA molecule as an antisense strand that is substantially complementary to the first RNA molecule (paragraphs 0015, 0032, 0128–0132, and 0136; and see Fig. 4). In one embodiment, both RNA Polymerase III promoters are separated from the RNA coding region by termination sequences, preferably termination sequences having five consecutive T residues (paragraphs 0015, 0032,

0128–0132, and 0136; and see Fig. 4). Lois-Caballe et al. teach that the RNA coding region may encode an RNA molecule that is capable of down-regulating the expression of a particular gene or genes (paragraph 0128) and is generally at least about at least about 15 nucleotides in length and is preferably about 15 to about 30 nucleotides in length (paragraph 0132). In a more preferred embodiment, the RNA duplex is between about 19 and 22 nucleotides in length (paragraph 0132).

Regarding claim 9 of the instant application, Lois-Caballe et al. further teach (paragraphs 0072 and 0082) that the viral construct may comprise sequences that serve as markers for the provirus, which sequences may be expressed in cells of a transgenic animal (paragraph 0076). Such sequences may encode reporter or marker proteins such as green fluorescent protein (0076 and 0082).

Regarding claim 10 and further regarding claims 11–13 of the instant application, Lois-Caballe et al. also teach (paragraph 0066 and 0071) that the viral construct comprises sequences necessary for the production of recombinant virus in a packaging cell, and that it may contain a promoter to increase the titer of the virus recovered from a cell line. This is interpreted to mean that upon infection of the appropriate cell line, the construct is replicated. Accordingly, the construct is expected to contain a replication origin, as required by claim 10 of the instant application. Furthermore, Lois-Caballe et al. teach that the viral construct is preferably cloned into a plasmid that may be transfected into a packaging cell line, and that the plasmid preferably comprises sequences useful for replication of the plasmid in bacteria (paragraphs 0089 and 0095). Thus, the plasmid, which contains the viral construct, also contains an origin of replication, meeting the limitation of claim 10 of the instant application.

Thus, Lois-Caballe et al. anticipate claims 1 and 6–13 of the instant application.

Furthermore, Lois-Caballe et al. anticipate Claims 14–16 because of the interpretation of the term "plurality," recited in claim 14. As explained above, the word "plurality" does not limit the structure of the vector but merely indicates that more than one vector or polynucleotide molecule must be present. The examiner submits that the applied reference, Lois-Caballe et al., meets this limitation since the construction of the disclosed vector in aqueous solution, according to conventional techniques, would invariably lead to the production of multiple copies of the vector.

> MPEP §2131.01 Multiple Reference 35 U.S.C. 102 Rejections
> Normally, only one reference should be used in making a rejection under 35 U.S.C. 102. However, a 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra references are cited to:
> (A) Prove the primary reference contains an "enabled disclosure;"
> (B) Explain the meaning of a term used in the primary reference; or
> (C) Show that a characteristic not disclosed in the reference is inherent.

The following supplemental references are relied on as part of the foregoing rejection under 35 USC 102(b):

Lodish et al. (1995) *Molecular Cell Biology*, 3rd ed to explain the meaning of the term "replication origin": a stretch of DNA that is necessary and sufficient for replication of a circular DNA molecule, usually a plasmid or virus, in an appropriate host cell (page 370).

Narayan and Clements (1989), *J. Gen. Virol.* 70:1617–1639 to show that a characteristic is inherent. Narayan and Clements state that the lentiviral genome is a positive-stranded polyadenylated RNA having 5' and 3' ends (page 1619-20). Moreover, it is stated that purine

rich sequences located upstream of the U3 regions serve as the initiation site for synthesis of plus strand DNA (page 1620).

These references support the contention that the lentiviral construct taught by Lois-Caballe et al. is a linear vector as required by claim 13, and that it contains sequences necessary for viral DNA replication, as required by claim 10.

*****

Claims 1–4, 6–16, and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Farmer (US 2005/0060771).

US 2005/0060771 claims the benefit of US provisional application 60/502,403, filed on Sept. 11, 2003.

Claims 1 and 6–16 are described above. Claims 2, 3, and 4 limit Claim 1 by stating that the vector further comprises a cleavage site for a restriction enzyme disposed within each of the first and second RNA polymerase termination signals (claim 2), wherein the cleavage site of the restriction enzyme is located outside the recognition site for the enzyme (claim 3). Furthermore, the restriction enzyme is an enzyme selected from the group of enzymes recited in claim 4, which includes BbsI, BsaI, and SapI. Independent Claim 33 recites a kit comprising an expression vector as also recited in claim 2, and packaging.

The term "packaging," as recited in claim 33, is interpreted in light of the instant application, which states (page 20):

> The expression vectors may be packaged in aqueous media or in lyophilized form. Exemplary packaging includes at least one container, such as a vial, tube, bottle, or other suitable container means, into which an expression vector may be placed.

The examiner notes that the enzymes recited in claim 4, including BbsI, BsaI, and SapI, are enzymes that cleave outside of their recognition site (see instant application at page 10-11). The examiner further notes that "enzymes that cleave outside their recognition site" are referred to in the art as Type IIS enzymes (see New England Biolabs online catalog printout, US 2005/0060771, and the Bath et al. reference cited below for the rejection under 35 USC 103).

Regarding claims 1 and 6–8, Farmer teaches siRNA encoding constructs comprising an siRNA coding domain flanked by opposing Pol III promoters and disposed between Pol III terminators (paragr. 0006–7; 0029, and 0036–0048; and see Figs. 1 and 2). The sense and antisense strands of the siRNA coding domain are said to be under transcriptional control of the opposing Pol III promoters flanking the domain (paragr. 0006 and 7). Furthermore, each of the promoters is operationally linked to a transcription terminator that is present in a non-transcribed region of each of said promoters and that is adjacent to the siRNA coding domain (paragraph 007 and 0041; see also Fig. 2). The siRNA coding domain is said to give rise to siRNA product molecules that range in length from about 10 to about 30–35 residues, from about 15 to about 25, or from 20 to about 23 residues (paragr. 0038).

Regarding claims 2–4, Farmer teaches that the constructs contain Type IIS restriction endonuclease sites within each of the RNA polymerase III termination signals (Fig. 2, paragraphs 0045, 46, and 101). Preferred restriction sites are said to be BbsI, BsaI, and SapI (paragraph. 0045 and 101).

Regarding claims 9–13, Farmer further teaches that the constructs may include a selectable marker, such as GFP (parag. 0047). Moreover, Farmer teaches that the constructs made up of a siRNA coding domain flanked by two opposing promoters are present on a vector.

The constructs may be present on any convenient type of vector, where representative vectors of interest include, but are not limited to: plasmid vectors and viral vectors, including lentivirus (paragr. 0042 and 0044), a linear vector as explained above. Farmer teaches that one type of vector is an episomal vector, i.e., a nucleic acid capable of extra-chromosomal replication in an appropriate host, e.g., a eukaryotic or prokaryotic host cell. Vectors capable of directing the expression of genes to which they are operatively linked are referred to herein as "expression vectors" (0016). Thus, Farmer clearly contemplates that such vectors will contain origins of replication as recited in Claim 10 of the instant application.

Similarly, Farmer's teachings encompass "a plurality" of vectors according to claims 14–16 of the instant application, meeting all the limitations of these claims for the reasons discussed above in the previous rejection.

Regarding claim 33, Farmer teaches that the vector constructs disclosed may be included in kits (see paragraphs 0093–0095), and that the vector constructs may be formulated into pharmaceutical compositions or preparations (parag. 0084, for example). Clearly, such disclosure contemplates the use of packaging within the meaning provided by the instant application (see above). It is clear that kits normally supply reagents in containers to keep the reagents sterile and to prevent the components from comingling and spilling.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Farmer (US 2005/0060771) and Bath et al. (2002) *J. Biol. Chem.* 277:4024–4033.

Claim 5 limits claim 4, described above, by stating that the restriction enzyme cleavage site present in the expression vector of claim 2 is one that is recognized by BsmBI, a type IIS restriction enzyme.

Farmer is relied upon for the reasons given above. Farmer teaches the use of Type IIS restriction sites and enzymes, including BbsI, BsaI, and SapI for use in constructing siRNA expression vectors, having opposing Pol III promoters operably linked to Pol III terminators, and

coding sequences disposed therebetween. Farmer does not specifically teach the use of the type IIS restriction endonuclease BsmBI.

Bath et al. teach BsmBI as well as many other Type IIS restriction endonucleases, including BsaI and SapI. A detailed analysis of the enzymatic activity and sequence specificity of BsmBI is presented (see Table 1, page 4026, and the section entitled DNA Cleavage by *BsmBI, BsmI, BsaI, and SapI*, beginning on page 4026). Specifically, Bath et al. state on page 4026 that "These enzymes were selected as examples of type IIs nucleases that cleave DNA close to their recognition sites, 1 bp away in one strand and [less than or equal to] 5 bp away in the other (Table I)." Bath et al. state that "BsmBI cleaved the supercoiled (SC) form of pBR322 directly to the full-length linear (FLL) form, without the accumulation of any of the nicked open-circle (OC) DNA during the course of the reaction (Fig. 2*a*). Hence, *Bsm*BI cuts its recognition site in both strands within a single DNA binding event." Overall, Bath et al. is considered to be an in depth guide as to the utility, activity, and specificity of BsmBI. Importantly, Bath et al. also teach BsaI and SapI, which were used by Farmer for the construction of siRNA Pol III expression vectors, as described above. According to Bath et al "When *Bsm*I, *Bsa*I, and *Sap*I were tested against the plasmids with one or with two copies of their respective recognition sites (reactions not shown), they all behaved in essentially the same manner as that shown for *Bsm*BI (Fig. 2)." (page 4027). Thus, the enzymes are art-recognized equivalents.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use BsmBI as taught by Bath et al. for cloning siRNA coding sequences into Pol III expression cassettes as taught by Farmer. One of ordinary skill in the art reading the Bath et al. reference would have recognized that BsmBI could be substituted for BsaI or SapI, as used by

Farmer, since Bath et al. specifically disclose that these three enzymes have similar activities and similar if not identical recognition sequences (Table I, Bath et al.). Moreover, they all cleave outside their recognition sequence. In short, the enzymes are art-recognized equivalents. In fact, applicants themselves disclose on pages 10–11, and in the Markush group of Claim 4, seem to suggest that BsmBI may be substituted for BsaI or SapI, or vice versa.

One would have been motivated to combine the Bath et al. and Farmer teachings since Farmer teaches (at paragraphs 0045 and 46) that while any convenient restriction endonuclease recognized sequence may be used for the insertion site, (and a multitude of such sequences are known in the art), of interest in many embodiments are sites recognized or cleaved by Type IIS restriction endonucleases. Farmer further states that representative known Type IIS restriction endonuncleases are SapI, bbsI, and BsaI. When using such proconstructs, the insertion site is first cleaved with the appropriate endonuclease, e.g., the appropriate Type IIS endonuclease. The desired siRNA coding sequence is then cloned into the site, e.g., using standard protocols.

In addition at paragraph 0101, Farmer states that Type IIS sites are preferred: "In addition, a SapI site (Type IIS restriction site) is added into the MC between the BamHI site and the Terminator. This SapI site is so positioned such that it will cut the DNA inside the promoter/terminator sequence--allowing the seemless cloning of gene-specific oligos for RNAi into the vector between the 2 promoters."

One would have had a reasonable expectation of success given that Farmer et al. teach that the use of Type IIS restriction enzymes are preferred because they enable one to conveniently construct Pol III-driven siRNA expression cassettes in a way that preserves the

termination signals and functional activity, such that following transfection into cells, the vectors produce target-specific inhibition of gene expression (paragraphs 0101–0115).

Thus in the absence of evidence to the contrary, the invention claimed in claims 1, 2, 4, and 5 as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Prior art of interest

The following prior art made of record and not relied upon in the preceding rejections is considered pertinent to applicant's disclosure.

Zheng et al. (2004) *PNAS* "An approach to genomewide screens of expressed small interfering RNAs in mammalian cells." 101:135–140. This reference describes siRNA expression vectors comprising opposing Pol III promoters and terminators for use in gene interference screens. (Cited in applicants' IDS).

Timmons and Fire (1998) *Nature* "Specific interference by ingested dsRNA" 395:854. The reference discloses a bacterial plasmid vector containing opposing T7 promoters for bidirectional transcription of dsRNA in bacteria, which produces RNA-mediated interference when ingested by *C. elegans*.

Fire et al. US Patent 6,506,559

Wang et al. (2000) *J. Biol. Chem.* "Inhibition of *Trypanosoma brucei* gene expression by RNA interference using an intergratable vector with opposing T7 promoters." 275:40174–40179.

Conclusion

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis V. Wollenberger whose telephone number is 571-272-8144. The examiner can normally be reached on Mon–Fri, 8:00 am–4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval system (PAIR). Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Louis V. Wollenberger, Ph.D.
Examiner
Art Unit 1635
August 19, 2005

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